UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,749	06/12/2001	Candace Pert	11496/9-1052	3948

7590 05/12/2003

William J Sapone
Coleman Sudol Sapone
708 Third Avenue
New York, NY 10017

EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 05/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/647,749	Applicant(s) PERT ET AL.
	Examiner Christopher Nichols, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *2-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Preliminary Amendment received 12 March 2002 (Paper No. 8) has been received and entered in full. Claims 1, 2, 4, 5, and 6 have been amended. Claims 1-7 are under examination.

2. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Drawings

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: the legend in the drawing lists peptide sequences, these must be accompanied by their respective SEQ ID NO's. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

4. The disclosure is objected to because of the following informalities: the specification recites amino acid sequences without the appropriate SEQ ID NO's (pp. 5 lines 5-6). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims **2-7** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. Claims 4-7 are broadly drawn to the use of SEQ ID NO: 1 and SEQ ID NO: 2 as therapeutic peptides for treating the symptoms of a disease causing neuronal cell death. Claims 2 and 3 are directed to SEQ ID NO: 1 and SEQ ID NO: 2 and pharmaceutical compositions thereof. The single intended use for pharmaceutical compositions is therapy. Since therapy is non-enabled, these claims are also totally non-enabled. Amendment of claims 2 and 3 to delete "pharmaceutical" may overcome this rejection for claims 2 and 3.

7. The specification teaches how to make and use SEQ ID NO: 1 and SEQ ID NO: 2 in an *in vitro* cell death assay involving gpl20.

8. A person skilled in the art would recognize that predicting the efficacy of a compound for therapeutic uses based solely on its performance *in vitro* is highly problematic. Thus, although the specification prophetically considers and discloses a particular mode of treatments for the claimed compositions, such a disclosure would not be considered enabling since the state of peptide therapeutics study is highly unpredictable, especially in neurology (or the field of disease associated with neuronal cell loss).

9. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

10. The following references are cited herein to illustrate the state of the art of neuropathology.

11. Buzy *et al.* (1992) "Potent gp120-like neurotoxic activity in the cerebrospinal fluid of HIV-infected individuals is blocked by peptide T." Brain Research **598**(1-2): 10-18 teaches that the dosages, toxic levels of gp120, and effects of peptide T on patients varies from those results gathered from in vitro assays (Figure 1B-1D and 2B). Therefore, sequence *in vitro* results cannot be relied upon solely and are unreliable for predication of *in vivo* or therapeutic applications. Buzy *et al.* further teaches that neuronal death or loss in AIDS CNS disease results from multiple factors, other than gp120 (pp. 15-16). Thus multiple factors are in play in any particular disorder and SEQ ID NO: 1 and SEQ ID NO: 2, while demonstrating action *in vitro* do not assure a skilled artisan of full effectiveness *in vivo*.

12. Offen *et al.* (2000) "Apoptosis as a general cell death pathway in neurodegenerative diseases." J. Neural. Transm. [Suppl] **58**: 153-166 teaches the apoptosis is a common form of cell loss in many neurodegenerative diseases (pp. 153-166). However, neither the Specification nor the prior art teaches the SEQ ID NO: 1 or SEQ ID NO: 2 may be involved in slowing or inhibiting apoptosis. Thus, it is not clear whether these peptides act on a common mechanism of cell loss shared by numerous neurodegenerative diseases (including by not limited to

Alzheimer's Disease, Parkinson's disease, Huntington's disease). The skilled artisan is therefore presented with no guidance as to how SEQ ID NO: 1 or SEQ ID NO: 2 would act on a key mechanism of neuronal loss in these diseases. Absent evidence of *in vivo* demonstration of the peptide's therapeutic properties, the skilled artisan is presented with an undue burden of experimentation in the face of an unpredictable art.

13. Brenneman *et al.* (13 October 1998) "Neuronal cell killing by the envelope protein of HIV and its prevention by vasoactive intestinal peptide." Nature **33**(6191): 639-642 teaches that secretin, a peptide with significant sequence homology and size similarity to vasoactive intestinal peptide (VIP), lacks the beneficial properties of promoting cell survival in an *in vitro* gp120-induced cell death model (Figure 3). Therefore, sequence homology cannot be relied upon solely to predict *in vitro* results and is especially unreliable for *in vivo* or therapeutic applications.

14. Sacerdote *et al.* (1987) "Vasoactive Intestinal Peptide 1-12: A Ligand for the CD4 (T4)/Human Immunodeficiency Virus Receptor." Journal of Neuroscience Research **18**(1): 102-107 teaches the peptide derivatives of VIP all differ in this actions and affinity for their receptor (Figures 1-4). This further demonstrates that sequence homology to a known beneficial peptide (VIP or peptide T) is not sufficient to predict activity or affinity for the endogenous receptor (Table I and III). Absent evidence of *in vivo* demonstration of the peptide's therapeutic properties, the skilled artisan is presented with an undue burden of experimentation in the face of an unpredictable art.

15. Due to the large quantity of experimentation necessary to identify all the applicable diseases involving neuronal loss and the applicable symptoms, the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating the effects of

SEQ ID NO: 1 and SEQ ID NO: 2 on all applicable diseases involving neuronal loss, the absence of working examples directed to known diseases involving neuronal loss, the complex nature of the invention, the unpredictability of the effects of SEQ ID NO: 1 and SEQ ID NO: 2 on cells and/or patients (see references and discussion above), and the breadth of the claims which fail to recite limitations for what constitutes an applicable relief of symptoms of diseases involving neuronal loss, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Summary

16. Claim 1 is allowable.

17. Claims 2-7 are hereby rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
May 5th, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER